REMARKS

Claims 1-89 have been canceled without prejudice and new claims 90-177 have been added. Thus, following entry of the amendments made herein, claims 90-177 will be pending in the present application.

Support for the new claims can be found, *inter alia*, in the paragraphs of U.S. Patent Publication No. 2003/0013091, the publication of the above-identified application, listed in the table below. No new matter has been added.

Claim	**Support**
90	[0006], [0008], [0017], [0028], [0029], [0027], [0079], [0080]
91	[0008], [0017], [0028], [0029], [0027], [0053], [0079], [0080]
92	[0008], [0017], [0028], [0029], [0027], [0078], [0079], [0080], [0082]
93	[0008], [0017], [0018], [0028], [0029], [0027], [0079], [0080]
94	[0008], [0017], [0024], [0028], [0029], [0027], [0079], [0080]
95, 113-119	[0008], [0011], [0071]
96, 99, 106, 155, 168	[0078]
97, 100, 102, 107, 109, 111, 112, 167	[0011]
98, 101, 103, 104, 105, 108	[0017], [0024]
110	[0011]
120	[0008]
121, 122	[0013], [0020]
123	[0011], [0017], [0024],
124, 158	[0017]
125	[0017]
126, 127	[0090]
128, 159,	[0036]-[0040]
129, 137, 154, 160	[0036]

Claim	Support
130	[0055]
131,	[0092]
132, 161	[0038]
133-135, 162-164	[0023], [0056]
136, 153	[0053]
138-141, 156	[0013]
142-150, 169-177	[0029], [0068], and [0082]
151	[0008], [0017], [0028], [0029], [0027], [0038], [0079], [0080]
152	[0008], [0017], [0028], [0029], [0027], [0079], [0080], [0090]
157	[0008], [0017], [0028], [0029], [0027], [0078], [0079], [0080], [0113]
165	[0011],
166	[0017], [0020]

THE REJECTIONS UNDER 35 U.S.C. § 102(e) SHOULD BE WITHDRAWN

Mirkin

Claims 1-12, 78, 80-82, 85-89 are rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,361,944 to Mirkin et al. ("Mirkin").

According to the Examiner, Mirkin teaches:

> ...a diverse population of labels, or unique probes comprising unique labels (each nanoparticle with plurality of oligonucleotide sequences each oligonucleotide having a reporter group) wherein each said unique label comprises at least two anti-gene digits (complementary sequences or oligonucleotide probe sequences) (see col. 22, line 11-23; col. 15, line 50-59; col. 32, line 44-67; col. 33, line 1-65; col. 26, line 56-67; col. 27, line 1-12, indicates one type of nanoparticles having oligonucleotide portions complementary to another type of nanoparticles having oligonucleotide sequences)).

Applicant notes at the outset that the rejected claims have been canceled and replaced by new claims 90-177.

Applicants respectfully submit that the Examiner has mischaracterized the teachings of Mirkin. Mirkin generally relates to detection of target nucleic acids using nanoparticle-bound oligonucleotides. In certain permutations of the detection methods disclosed by Mirkin, the nanoparticle-bound oligonucleotides are hybridized to labeled oligonucleotides that contain target-specific sequences to form target-specific probes, as outlined in Figure 24. In other permutations, as outlined in Figure 28, the nanoparticle-bound oligonucleotides ("a" in Figure 28A-B) are hybridized to complementary nanoparticle-bound oligonucleotides ("a^1" in Figure 28A-B), forming "core particles," and these core particles in turn are hybridized to yet a third set of complementary nanoparticle-bound oligonucleotides, the nanoparticles to which this third set of oligonucleotides are attached containing an additional set of target-specific oligonucleotides ("b" in Figure 28A-B), to form an "aggregate" target-specific probe.

It is axiomatic that for a prior art reference to anticipate a claimed invention under 35 U.S.C. § 102, it has to meet every element of the claimed invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). Nowhere in Mirkin is there a teaching, or even a suggestion, of the presently claimed invention. Of the new claims, claims 90-94, 151, 152, and 157 are independent. Mirkin does not teach each and every element of any of the independent claims, nor does Mirkin render obvious any of these claims, as discussed below.

Nowhere in the disclosure of Mirkin is there a teaching or suggestion of a population of thirty or more (as claimed in claims 90-94 and 151) or one hundred or more (as claimed in claim 152) unique labels, each comprising a molecule with a plurality of genedigits, in which at least two genedigits (or, in the case of claim 152, at least four genedigits) are each attached to a respective anti-genedigit, each anti-genedigit being attached to at least one label monomer, as required by the claims. In particular, Mirkin does not teach a population of 30 more unique labels as specified in the claims. At column 16, lines 29-36, Mirkin teaches a variety of different types of nanoparticles that can be used. However, only 24 different nanoparticles are listed and, importantly, there is no suggestion to create a population of such labels (nor whether each label in the 24 would be unique - *i.e.*, distinguishable from the others) (see ¶ 21 of U.S. Patent Publication No. 2003/0013091). In contrast, Mirkin suggests selecting one particular type of

nanoparticle label, gold, for preferred use (col. 16, lines 64-65). Thus, Mirkin does not teach or suggest the subject matter of any of independent claims 90-94, 151 and 152.

With respect to claim 157, Mirkin does not teach or suggest a labeling kit comprising in one container thirty or more unique molecules with a plurality of genedigits of predetermined sequence and in one or more other containers a plurality of respective anti-genedigits, each attached to at least one label monomer, for the same reasons as discussed above. Thus, Mirkin also does not teach or suggest the subject matter of independent claim 157.

Further, in view of the novelty of independent claims 90-94, 151, 152, and 157 over Mirkin, it is axiomatic that their dependent claims are also novel over Mirkin.

Krantz

Claims 1, 4, and 6 are rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,277,583 to Krantz et al. ("Krantz").

According to the Examiner, Krantz teaches:

> ... a diverse population of claim 1, comprising a library of unique labels (a library includes plurality of affinity labels), wherein each unique label comprises at least two anti gene digits (complementary sequences) (see col. 6, line 30-57, col. 4, line 3-7, indicates one oligomer monomer portion is complementary to another one of a number of different monomers of the same type (gene digit) and another portion is complementary to the target sequence (gene digit);
>
> With regard to claim 4, unique labels having diversity selected from a group consisting of at least about 100 to 10,000 of more members (see col. 6, line 46-50);
>
> With regard to claim 6, the labels are fluorescent (see col. 9, line 43-50).

Applicant respectfully disagrees with the Examiner's rejection. Krantz teaches methods of generating combinatorial libraries of affinity tags by constructing oligomeric molecules with functional groups. Thus, in its preferred embodiment, Krantz teaches a method of constructing oligomers with different permutations of monomers in a stepwise fashion. In one embodiment, the monomers are nucleotides, and the oligomers thus constructed are oligonucleotides (see, *e.g.*, Krantz at column 6, lines 30-50). A preferred application of this method is presented at column

7, lines 6-21 of Krantz, which describes an example of a library of oligopeptides, each of the members having a common terminus of 2-3 amino acids and a variety of random di- or tri-peptides at successive positions. In one embodiment, the affinity tags are detectably labeled (column 9, lines 40-50). However, contrary to the Examiner's assertions, Krantz does not teach or suggest a population of thirty or more (as claimed in claims 90-94 and 151) or one hundred or more (as claimed in claim 152) unique labels, nor does Krantz teach or suggest a labeling kit comprising in one container thirty or more unique molecules (as claimed in claim 157).

As discussed above, it is axiomatic that for a prior art reference to anticipate a claimed invention under 35 U.S.C. § 102, it has to meet every element of the claimed invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). Krantz does not teach each and every element of any of independent new claims 90-94, 151, 152, and 157, nor does Krantz render obvious any of these claims.

Nowhere in the disclosure of Krantz is there a teaching or suggestion of a population of thirty or more (as claimed in claims 90-94 and 151) or one hundred or more (as claimed in claim 152) unique labels, each comprising a molecule with a plurality of genedigits, in which at least two genedigits (or, in the case of claim 152, at least four genedigits) are each attached to a respective anti-genedigit, each anti-genedigit being attached to at least one label monomer, as required by the claims. The so-called affinity "labels" taught by Krantz are not "labels," as that term is used in the instant specification (see ¶ 20 of U.S. Patent Publication No. 2003/0013091). Instead, the affinity "labels" of Krantz are molecules from a combinatorial library that preferentially bind to a macromolecular target of interest (Krantz at col. 4, lines 1-15 and 38-50). Krantz does teach that the affinity "labels" can be labeled with detectable groups such as fluorescers, radiolabels, etc. (see col. 9, lines 43-64; see also col. 8, lines 55-59). However, there is no teaching or suggestion in Krantz of a population of 30 or more unique labels as specified in the claims. In particular, there is no suggestion of creating a population of 30 or more unique labels.

Krantz also does not teach or suggest a labeling kit comprising in one container thirty or more unique molecules with a plurality of genedigits of predetermined sequence and in one or

more other containers a plurality of respective anti-genedigits, each attached to at least one label monomer, as claimed in independent claim 157, for reasons stated above. Thus, Krantz does not teach or suggest the subject matter of any of independent claims 90-94, 151, 152 and 157.

Further, in view of the novelty of independent claims 90-94, 151, 152, and 157 over Krantz, it is axiomatic that their dependent claims are also novel over Krantz.

CONCLUSION

Applicant respectfully requests that the Examiner reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned agent if a telephone call would help resolve any remaining items.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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